

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

---

IN RE APPLICATION OF: Zheng J. Li, et al.	:	
APPLICATION NO.: 10/650,253	:	Examiner: PESELEV, ELLI
FILING DATE: AUGUST 27, 2003	:	Group Art Unit: 1623
TITLE: CRYSTAL FORMS OF AZITHROMYCIN		

---

Commissioner for Patents  
P.O. Box 1450  
Alexandria, VA 22313-1450

Sir:

DECLARATION UNDER RULE §131

I, Richard Todd Darrington, declare that:

1. I received my Doctor of Philosophy degree in Pharmaceutical Chemistry from the University of Utah in December 1993.
2. Since December 1993, I have worked for Glaxo Inc., Pfizer, Inc. in Groton-CT and Boehringer Ingelheim to study new pharmaceutical formulations.
3. During my tenure at Pfizer, Inc. and prior to May 8, 1998, I participated in the conception and reduction to practice of a pharmaceutical dosage form containing substantially pure Form F azithromycin (referred to as "ethanol solvate Lot 34503-138-1" in the notebook which is attached herein as exhibit 1). Exhibit 1 includes two pages, one page from my notebook and one from that of William N. Soby who worked under my supervision at the time. Exhibit 1 is redacted as to the dates which all occurred before May 8, 1998.
4. Exhibit 1 describes a pharmaceutical dosage form containing ethanol solvate (Lot 34503-138-1) and a pharmaceutically acceptable carrier, Miglyol 812. The dosage form was made prior to May 8, 1998.

EXPRESS MAIL NO. EV6548054360US<sup>1</sup>

5. I further declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issuing thereon.

  
\_\_\_\_\_  
RICHARD TODD DARRINGTON

July 11, 2005  
DATE

cat for 37791-79  
Nº 37791- 80

cont.



EtOH Solvate Lot 34503-138-1

Calculations for Mass of Drug or Salt-Percentage by Weight Method					
Drug Form (salt)	EtOH Solvate	Drug Form	Molecular Weight	Density mg/mL	Percent Purity
Lot Number	34503-138-1				
		Azithromycin	785	1.132	92.7
Percent Purity	91.9	Azithromycin HCl	821.5	1.170	100
Density (g/mL)	1.132	Azithromycin HCl	821.5		89.5
		Azithromycin 2HCl	858	1.178	100
Vehicle	Miglyol 812	Monopamoate Salt	1137.36		63.5
Lot Number		Monopamoate Salt	1137.36	1.577	61.8
		Monocamsylate Salt	981.31		
Desired Activity* (mg/mL)	100	Decanote	921.23	1.210	86.14
Target Volume (mL)	35.0	Mesylate Salt			88.62
Mass of Drug to Add	3.8089				
Volume Occupied by Drug	3.36				
Volume of Vehicle to Add	31.64				
*Based on azithromycin dihydrate					

At 74 (vid 2) 3.8086g.

We distributed while receiving oil and did not record.  
Since we are low on Silicate do not have enough to re-do  
will have to estimate and use APID primary determination.

miglyol 812 10g

bulk all 40m

miglyol 812 21.712g

Lot # 37791-80-1 A suspension  
of Azithromycin ethanol solvate  
(CP-62,993-4x) in Miglyol at 100  
mg/mL Prepared

*[Signature]*  
Eam Aronson

BEST AVAILABLE COPY



No 38548-32

Quick Solubility Screen on New Salts (Continued from page 29)

Vial Number	Salt	Lot Number	Empty Mass of Vial (g)	Mass with Salt (g)	Mass of Salt (mg)	Weighted Mass of Salt (mg)	Final Mass (g)
1	CP-62,993-13	34503-140-1	6.2358	6.2458	10.00	10.1516	6.4939
2	CP-62,993-13	34503-140-1	6.3848	6.395	10.20	10.5063	10.1934
3	CP-62,993-42	34503-143-1	6.3208	6.3307	9.90	10.576	6.4299
4	CP-62,993-42	34503-143-1	6.3375	6.3481	10.60	11.297	10.2201
5	CP-62,993-7	34503-138-1	6.3127	6.3222	9.50	9.947	10.1012
6	CP-62,993-7	34503-138-1	6.3135	6.3237	10.20	10.7387	8.8458
7	CP-62,993-42	34503-143-2	6.2838	6.2960	12.20	12.0788	6.4937
8	CP-62,993-42	34503-143-2	6.3098	6.3210	11.20	11.3050	10.1028
9	CP-62,993-7	34503-138-2	6.2980	6.3085	10.50	10.5348	10.4763
10	CP-62,993-7	34503-138-2	6.3159	6.3267	10.80	10.8293	10.1026
2a	CP-62,993-13	34503-140-1	9.8518	9.856	4.20	4.1314	17.3513
4a	CP-62,993-42	34503-143-1	9.7591	9.7633	4.20	4.0303	17.2801
5a	CP-62,993-7	34503-138-1	9.7762	9.7807	4.50	4.4201	17.7722

Page 38548-32

Vial Number	Salt	Lot Number	Mass of Solvent (g)	Calculated Volume Added (uL)	Measured Volume (uL)	Solvent	Solubility
1	CP-62,993-13	34503-140-1	0.2481	249	250	Water	40.61
2	CP-62,993-13	34503-140-1	3.7984	4037	4000	Miglyol 812	2.63
3	CP-62,993-42	34503-143-1	0.0992	100	100	Water	105.76
4	CP-62,993-42	34503-143-1	3.872	4115	4000	Miglyol 812	2.82
5	CP-62,993-7	34503-138-1	3.779	3800	4000	Water	2.49
6	CP-62,993-7	34503-138-1	2.5221	2680	2600	Miglyol 812	4.13
7	CP-62,993-42	34503-143-2	0.1977	199	200	Water	60.39
8	CP-62,993-42	34503-143-2	3.7818	4019	4000	Miglyol 812	2.83
9	CP-62,993-7	34503-138-2	4.1678	4190	4000	Water	2.63
10	CP-62,993-7	34503-138-2	3.7759	4013	4000	Miglyol 812	2.71
2a	CP-62,993-13	34503-140-1	7.4953	7965	8000	Miglyol 812	0.52
4a	CP-62,993-42	34503-143-1	7.5168	7988	8000	Miglyol 812	0.50
5a	CP-62,993-7	34503-138-1	7.9915	8035	8000	Water	0.55

Page 38548-32

Continued on page 33

Signed: *William T. Loh*  
Witnessed: *Shing Shing*  
Witnessed:

Date:

Date:

Date:

BEST AVAILABLE COPY